ABSTRACT
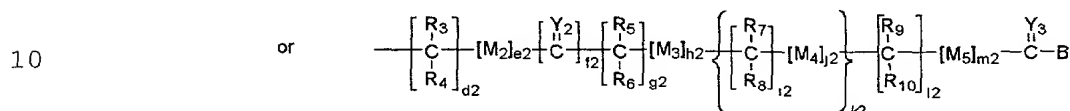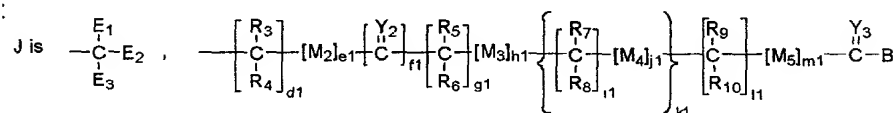
The present invention is directed to polymeric-prodrug transport forms of

the formula:

(I)

$$G \left[\begin{array}{c} R_1 \\ | \\ C \\ | \\ R_2 \end{array} \right]_a [M_1]_b \left[\begin{array}{c} Y_1 \\ || \\ C \end{array} \right]_c N \begin{array}{c} E_4 \\ \diagdown \\ J \end{array}$$

wherein:

J is $-\overset{\overset{\displaystyle E_1}{|}}{\underset{\underset{\displaystyle E_3}{|}}{C}}-E_2$,

$$-\left[\begin{array}{c}R_3\\|\\C\\|\\R_4\end{array}\right]_{d1}[M_2]_{e1}\left[\begin{array}{c}Y_2\\||\\C\end{array}\right]_{f1}\left[\begin{array}{c}R_5\\|\\C\\|\\R_6\end{array}\right]_{g1}[M_3]_{h1}\left\{\left[\begin{array}{c}R_7\\|\\C\\|\\R_8\end{array}\right]_{i1}[M_4]_{j1}\right\}_{k1}\left[\begin{array}{c}R_9\\|\\C\\|\\R_{10}\end{array}\right]_{l1}[M_5]_{m1}\overset{Y_3}{\overset{||}{C}}-B$$

or

$$-\left[\begin{array}{c}R_3\\|\\C\\|\\R_4\end{array}\right]_{d2}[M_2]_{e2}\left[\begin{array}{c}Y_2\\||\\C\end{array}\right]_{f2}\left[\begin{array}{c}R_5\\|\\C\\|\\R_6\end{array}\right]_{g2}[M_3]_{h2}\left\{\left[\begin{array}{c}R_7\\|\\C\\|\\R_8\end{array}\right]_{i2}[M_4]_{j2}\right\}_{k2}\left[\begin{array}{c}R_9\\|\\C\\|\\R_{10}\end{array}\right]_{l2}[M_5]_{m2}\overset{Y_3}{\overset{||}{C}}-B$$
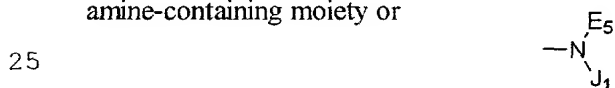
E_{1-4} are independently selected from the group consisting of hydrogen,

C_{1-6} alkyls, C_{3-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls,

C_{3-8} substituted cycloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} heteroalkyls,

substituted C_{1-6} heteroalkyls, C_{1-6} alkoxy, phenoxy, C_{1-6} heteroalkoxy,

$$-\left[\begin{array}{c}R_3\\|\\C\\|\\R_4\end{array}\right]_{d1}[M_2]_{e1}\left[\begin{array}{c}Y_2\\||\\C\end{array}\right]_{f1}\left[\begin{array}{c}R_5\\|\\C\\|\\R_6\end{array}\right]_{g1}[M_3]_{h1}\left\{\left[\begin{array}{c}R_7\\|\\C\\|\\R_8\end{array}\right]_{i1}[M_4]_{j1}\right\}_{k1}\left[\begin{array}{c}R_9\\|\\C\\|\\R_{10}\end{array}\right]_{l1}[M_5]_{m1}\overset{Y_3}{\overset{||}{C}}-B$$

or

$$-\left[\begin{array}{c}R_3\\|\\C\\|\\R_4\end{array}\right]_{d2}[M_2]_{e2}\left[\begin{array}{c}Y_2\\||\\C\end{array}\right]_{f2}\left[\begin{array}{c}R_5\\|\\C\\|\\R_6\end{array}\right]_{g2}[M_3]_{h2}\left\{\left[\begin{array}{c}R_7\\|\\C\\|\\R_8\end{array}\right]_{i2}[M_4]_{j2}\right\}_{k2}\left[\begin{array}{c}R_9\\|\\C\\|\\R_{10}\end{array}\right]_{l2}[M_5]_{m2}\overset{Y_3}{\overset{||}{C}}-B$$
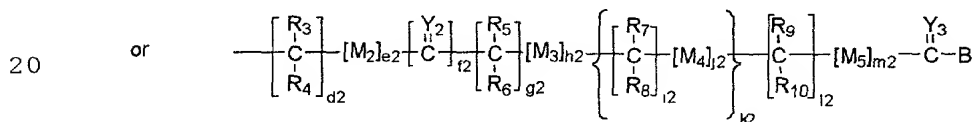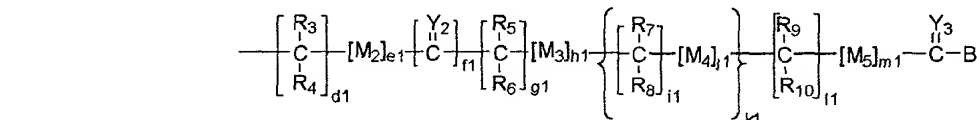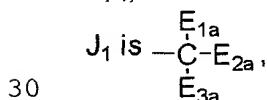
and at least one of E_{1-4} includes a B moiety;

B is a leaving group, OH, a residue of a hydroxyl-containing moiety, a residue of an
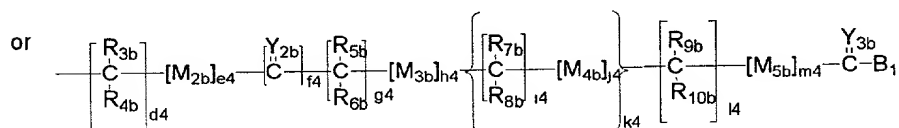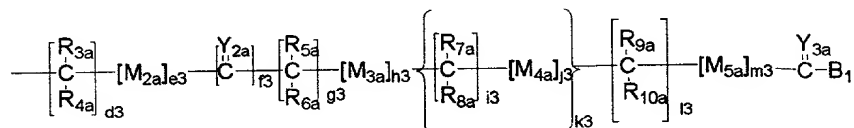
amine-containing moiety or $-N\begin{array}{c} E_5 \\ \diagup \\ \diagdown \\ J_1 \end{array}$

wherein E_5 is independently selected from the same group which defines

E_{1-4};

J_1 is $-\overset{\overset{\displaystyle E_{1a}}{|}}{\underset{\underset{\displaystyle E_{3a}}{|}}{C}}-E_{2a}$,

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E_{1a-3a} are independently selected from the group consisting of hydrogen, C_{1-6} alkyls, C_{3-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls, C_{3-8} substituted cycloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} heteroalkyls, substituted C_{1-6} heteroalkyls, C_{1-6} alkoxy, phenoxy, C_{1-6} heteroalkoxy,

$$-\left[\begin{array}{c}R_{3a}\\|\\C\\|\\R_{4a}\end{array}\right]_{d3}-[M_{2a}]_{e3}-\left[\begin{array}{c}Y_{2a}\\||\\C\end{array}\right]_{f3}\left[\begin{array}{c}R_{5a}\\|\\C\\|\\R_{6a}\end{array}\right]_{g3}-[M_{3a}]_{h3}\left\{\left[\begin{array}{c}R_{7a}\\|\\C\\|\\R_{8a}\end{array}\right]_{i3}-[M_{4a}]_{j3}\right\}_{k3}\left[\begin{array}{c}R_{9a}\\|\\C\\|\\R_{10a}\end{array}\right]_{l3}-[M_{5a}]_{m3}-\begin{array}{c}Y_{3a}\\||\\C\end{array}-B_1$$

or

$$-\left[\begin{array}{c}R_{3b}\\|\\C\\|\\R_{4b}\end{array}\right]_{d4}-[M_{2b}]_{e4}-\left[\begin{array}{c}Y_{2b}\\||\\C\end{array}\right]_{f4}\left[\begin{array}{c}R_{5b}\\|\\C\\|\\R_{6b}\end{array}\right]_{g4}-[M_{3b}]_{h4}\left\{\left[\begin{array}{c}R_{7b}\\|\\C\\|\\R_{8b}\end{array}\right]_{i4}-[M_{4b}]_{j4}\right\}_{k4}\left[\begin{array}{c}R_{9b}\\|\\C\\|\\R_{10b}\end{array}\right]_{l4}-[M_{5b}]_{m4}-\begin{array}{c}Y_{3b}\\||\\C\end{array}-B_1$$

wherein B_1 is a leaving group, OH, a residue of a hydroxyl-containing moiety or a residue of an amine-containing moiety or

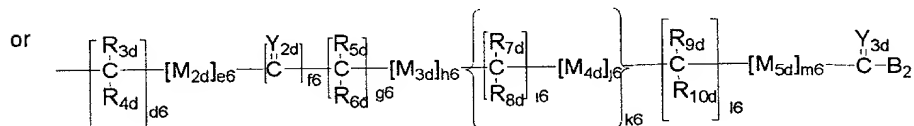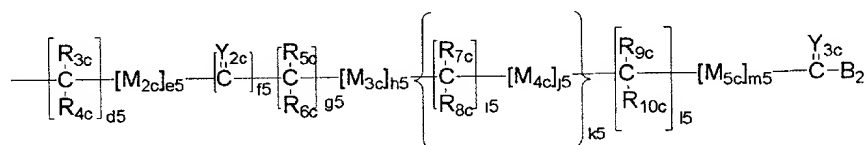$$-N\begin{array}{c}E_6\\ \\J_2\end{array}$$

wherein E_6 is independently selected from the same group which defines E_{1-4};

$$J_2 \text{ is } -\begin{array}{c}E_{1b}\\|\\C\\|\\E_{3b}\end{array}-E_{2b},$$
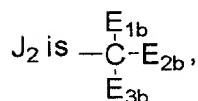
wherein E_{1b-3b} are independently selected from the group consisting of hydrogen, C_{1-6} alkyls, C_{3-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls, C_{3-8} substituted cycloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} heteroalkyls, substituted C_{1-6} heteroalkyls, C_{1-6} alkoxy, phenoxy, C_{1-6} heteroalkoxy,

$$-\left[\begin{array}{c}R_{3c}\\|\\C\\|\\R_{4c}\end{array}\right]_{d5}-[M_{2c}]_{e5}-\left[\begin{array}{c}Y_{2c}\\||\\C\end{array}\right]_{f5}\left[\begin{array}{c}R_{5c}\\|\\C\\|\\R_{6c}\end{array}\right]_{g5}-[M_{3c}]_{h5}\left\{\left[\begin{array}{c}R_{7c}\\|\\C\\|\\R_{8c}\end{array}\right]_{i5}-[M_{4c}]_{j5}\right\}_{k5}\left[\begin{array}{c}R_{9c}\\|\\C\\|\\R_{10c}\end{array}\right]_{l5}-[M_{5c}]_{m5}-\begin{array}{c}Y_{3c}\\||\\C\end{array}-B_2$$

or

$$-\left[\begin{array}{c}R_{3d}\\|\\C\\|\\R_{4d}\end{array}\right]_{d6}-[M_{2d}]_{e6}-\left[\begin{array}{c}Y_{2d}\\||\\C\end{array}\right]_{f6}\left[\begin{array}{c}R_{5d}\\|\\C\\|\\R_{6d}\end{array}\right]_{g6}-[M_{3d}]_{h6}\left\{\left[\begin{array}{c}R_{7d}\\|\\C\\|\\R_{8d}\end{array}\right]_{i6}-[M_{4d}]_{j6}\right\}_{k6}\left[\begin{array}{c}R_{9d}\\|\\C\\|\\R_{10d}\end{array}\right]_{l6}-[M_{5d}]_{m6}-\begin{array}{c}Y_{3d}\\||\\C\end{array}-B_2$$

wherein B_2 is a leaving group, OH, a residue of a hydroxyl-containing moiety or a residue of an amine-containing moiety;

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G is a polymeric residue;

Y_{1-3}, Y_{2a-d} and Y_{3a-d} are each independently O, S or NR_{11a}

M_{1-4}, M_{2a-2d}, M_{3a-3d}, and M_{4a-4d} are each independently O, S or NR_{11b};

M_5 and M_{5a-d} are each independently X or Q,

wherein X is an electron withdrawing group and Q is a moiety containing a free electron pair positioned three to six atoms from $C(=Y_3)$ or $C(=Y_{3a-d})$;

R_{1-10}, R_{1a-11a}, R_{1b-11b}, R_{1c-10c} and R_{1d-10d} are each independently selected from the group consisting of hydrogen, C_{1-6} alkyls, C_{3-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls, C_{3-8} substituted cycloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} heteroalkyls, substituted C_{1-6} heteroalkyls, C_{1-6} alkoxy, phenoxy and C_{1-6} heteroalkoxy; and

a, b, c, d1- d6, e1-e6, f1- f6, g1- g6, h1- h6, i1- i6, j1- j6, k1- k6, l1- l6, m1- m6 are each independently zero or a positive integer.

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